

INFLUENCE OF SMOKING FEWER CIGARETTES ON EXPOSURE TO TAR, NICOTINE, AND CARBON MONOXIDE

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Abstract In the hope of reducing the adverse health consequences of smoking, physicians frequently advise their patients who cannot quit to smoke fewer cigarettes. Habitual smokers may compensate for the reduced number of cigarettes, however, by taking in more smoke per cigarette. We measured the intake of tar (estimated as mutagenic activity of the urine), nicotine, and carbon monoxide during short-term cigarette restriction. With a reduction from an average of 37 cigarettes to an average of 5 cigarettes per day, the intake of tobacco tox-

ins per cigarette increased roughly threefold and daily exposure to tar and carbon monoxide declined only 50 percent.

We conclude that smoking fewer cigarettes may reduce exposure to toxins and related adverse health consequences. However, consistent with a tendency to maintain intake of nicotine, the magnitude of the benefit is much less than expected. Whether "oversmoking" persists during long-term restriction of cigarettes requires further investigation. (N Engl J Med 1986; 315:1310-3.)

WHEN faced with smokers who refuse to stop smoking, physicians frequently advise their patients, to switch to low-yield brands and to cut down on the number of cigarettes smoked daily. Recent research, however, has shown that switching to low-yield cigarettes is of limited value, because smokers compensate for lower yields by increasing their intake of mainstream smoke from each cigarette.¹⁻³ The recommendation to smoke fewer cigarettes is reasonable, being based on early epidemiologic studies indicating that the risks of lung cancer and coronary heart disease are proportional to daily cigarette consumption.^{4,5} When the number of cigarettes smoked is reduced, however, it is expected that the smoker will compensate by altering his or her smoking behavior to take in more smoke per cigarette.

One experimental study on this topic⁶ used single measurements of plasma nicotine and carboxyhemoglobin concentrations after cigarette smoking in a field experiment and found that restricting the smoking rate by 50 percent (from 29 to 15 cigarettes per day, on average) resulted in higher nicotine levels and unchanged carboxyhemoglobin levels after the restriction. However, this study could not assess overall changes in the body burden of toxins, did not examine the effects of restriction to 10 or fewer cigarettes per day, and did not confirm how well subjects complied with the request to reduce the number of cigarettes that they smoked. We therefore examined daily intake and intake per cigarette of tar (estimated as mutagenic activity of the urine),⁷ nicotine, and carbon monoxide, as well as smokers' satisfaction during cigarette restriction (down to five cigarettes per day) in a controlled environment.

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METHODS

We studied 13 paid volunteers, 10 men and 3 women 22 to 61 years old (mean, 37). They smoked an average of 39 cigarettes per day (range, 20 to 60) and had smoked for an average of 21 years (range, 3 to 49). The average Federal Trade Commission smoking-machine yields of the subjects' usual brands of cigarettes were 17.3 mg of tar, 1.1 mg of nicotine, and 14.9 mg of carbon monoxide. The subjects were hospitalized at the Clinical Study Center of San Francisco General Hospital for the duration of the study.

The subjects were studied in four experimental smoking blocks. Each block lasted three or four days. In the first block, the subjects smoked their own brand of cigarettes as they desired. In the next three blocks, they were given 15, 10, or 5 cigarettes of their usual brand to smoke per day. The order of the blocks was balanced by Latin square. The subjects were told that they were participating in a study of the health effects of smoking different numbers of cigarettes. They were also told that they could smoke their allotted cigarettes in any manner they wished, at any time of day.

All cigarette butts were collected. Urine was collected every 24 hours for determination of mutagenicity. Urine samples were stored at -20°C in polypropylene bottles for two weeks at most before extraction. Once during each study block, an indwelling butterfly catheter was inserted into the forearm vein for the collection of blood samples. Blood samples were collected every two hours from 8 a.m. to midnight, then at 4 a.m. and 8 a.m. the next day.

The concentrations of nicotine in the blood and urine were measured by gas-liquid chromatography.⁸ Carboxyhemoglobin was measured with an IL Model 280 co-oximeter.

The mutagenicity of the urine was measured according to a modification of the assay described by Yamasaki and Ames.⁹ Urine concentrates were prepared by pouring 100 ml of urine over a 6-ml octadecyl (C18) extraction column washed with distilled water. This was eluted with methanol, dried under nitrogen, and taken up into dimethylsulfoxide; the result was tested for mutagenic activity by the salmonella-histidine auxotroph-reversion assay (Ames salmonella strain TA98). Samples were tested in the presence of an Aroclor 1254-induced (S9) fraction of rat liver. The average number of histidine-independent revertants (bacterial colonies that have reverted from dependence on, to independence from, histidine) on duplicate plates on each of the last two days of each smoking block was computed. Earlier studies in our laboratory (Benowitz NL, et al.; unpublished data) have shown that values for urinary mutagenicity during abstinence from tobacco are similar to values for dimethylsulfoxide control procedures. Urinary mutagenic activity attributable to cigarette smoking was therefore computed as the difference between the number of revertants per 25 ml of urine during smoking and the number in the dimethylsulfoxide control.

Assays for urinary mutagenic activity during all experimental blocks of a subject were run on the same day. Mechanisms to control for day-to-day variability in the assay included two known positive controls: 2-aminofluorene and a sample of pooled smokers' urine. The mutagenic activity of the urine of 11 of the smokers was always at least twice that of the control sample. The urine of two

subjects had endogenous antibacterial activity, so that the assay could not be performed. Analyses of differences in mutagenic activity among the blocks were performed for 11 subjects. Since all urine samples from any given subject were analyzed on the same day, each subject served as his or her own control for changes that occurred during processing.

Exposure to nicotine and carbon monoxide was expressed as the area under the blood concentration-time curve for nicotine or carboxyhemoglobin over 24 hours. The carboxyhemoglobin value for a nonsmoker — 1 percent — was subtracted from all values, so that carbon monoxide exposure attributable to smoking could be computed. Daily mutagen excretion was computed by multiplying the number of revertant colonies per milliliter of urine by the 24-hour urine volume. Differences between experimental conditions were tested by repeated-measures analysis of variance, with Tukey post-tests.

RESULTS

During unrestricted smoking, the subjects smoked an average of 37 cigarettes per day. With a reduction in the number of cigarettes smoked, the 24-hour urinary mutagenic activity and exposure to nicotine and carbon monoxide declined, but proportionately less than the change in cigarette consumption (Table 1, Fig. 1). When smoking was restricted to five cigarettes a day, there was a 3.4-, 2.7-, and 3.2-fold increase in urine mutagenic activity and intake of nicotine and carbon monoxide per cigarette, respectively (Table 1), as compared with values during unrestricted smoking.

When subjects smoked 10 or 15 cigarettes per day (30 to 45 percent of base-line consumption), their blood nicotine concentrations were 60 to 70 percent of base line. When they smoked five cigarettes per day (15 percent of base-line consumption), their nicotine intake was reduced to 40 percent of base line (Fig. 1). The ratio of the area under the blood concentration-time curve for carbon monoxide (AUC_{CO}) to that for nicotine (AUC_{nic}) and the ratio of urinary mutagenic

activity to AUC_{nic} increased as fewer cigarettes were smoked, consistent with more frequent or intense puffing. The overall reduction in consumption from 37 to 5 cigarettes per day resulted in only a 50 percent reduction in exposure to tar and carbon monoxide.

Exposure to nicotine in individual subjects is shown in Figure 2. In the majority of smokers, nicotine exposure declined less than predicted by the number of cigarettes smoked between unrestricted smoking and smoking 15 cigarettes per day. In four subjects — those with the highest levels of nicotine intake — the expected magnitude of decline was observed. Three of the four with the lowest level of nicotine intake either did not change or increased their nicotine intake when they were restricted to 15 cigarettes per day.

To explore the possibility that the response to a reduction in the number of cigarettes smoked was influenced by the initial smoking rate, we examined correlations between the number of cigarettes smoked during unrestricted smoking and various measures of exposure. There were no significant correlations between the number of cigarettes smoked and AUC_{nic} when smoking was unrestricted ($r = 0.01$) or between the number of cigarettes smoked and the change in AUC between unrestricted smoking and smoking 15 cigarettes per day — whether as an absolute change ($r = 0.19$) or as a percentage change ($r = 0.13$). Smokers with a higher nicotine intake (AUC_{nic}) during unrestricted smoking did have a greater decline in AUC_{nic} when they were restricted to 15 cigarettes per day ($r = -0.77$; $P < 0.01$).

Twelve of the subjects were asked what it was like to restrict their cigarette smoking. None reported difficulty with smoking 15 cigarettes. Some sample comments were that there were "no difficulties," or "no hardship," and that it was "very easy." Four subjects

reported difficulties when smoking 10 cigarettes (two subjects found this regimen the most difficult). Eight subjects reported problems with smoking only five cigarettes (two subjects said that it would have been easier to stop smoking). The differences in the proportions of complaints from smokers during the 15-, 10-, and 5-cigarette smoking blocks were statistically significant.

DISCUSSION

On average, smokers greatly increased their intake of nicotine and other toxins per cigarette as the number of cigarettes that they smoked per day was reduced. As a consequence, the potential health benefit of the reduction in daily exposure to tobacco-related toxins was much less than a linear relation

Table 1. Influence of Cigarette Restriction on Urinary Mutagenic Activity and Exposure to Nicotine and Carbon Monoxide.

	CIGARETTE UNRESTRICTED (37±9/DAY)	CIGARETTES RESTRICTED		
		15/DAY	10/DAY	5/DAY
		mean ±SD		
Urinary mutagenic activity (UMA) — no. of revertants				
Per 24 hr	13,626±3852	11,555±2926	9514±1881*	8830±1247*†
Per cigarette	257±102	472±195*	507±238*	879±216*††
Nicotine exposure (AUC_{nic}) — ng/ml-hr				
Per 24 hr	516±187	349±121*	278±156*	196±128*†
Per cigarette	14.1±5.6	22.6±8.1*	28.3±16.2*	38.8±26.7*†
Carbon monoxide exposure (AUC_{CO}) — %-hr				
Per 24 hr	186±66	137±30*	107±20*	81±151*†
Per cigarette	5.1±2.0	8.9±1.9*	10.5±1.9*	16.1±2.9*††
UMA/ AUC_{nic}	19.9±9.0	29.4±8.9	20.3±12.8	27.6±14.0§
AUC_{CO}/AUC_{nic}	0.38±0.13	0.44±0.18	0.45±0.19	0.54±0.26*

*Significantly different from value for unrestricted cigarettes ($P < 0.05$).

†Significantly different from value for 15 cigarettes per day ($P < 0.05$).

††Significantly different from value for 10 cigarettes per day ($P < 0.05$).

§ $P = 0.06$ for the comparison with all other values for UMA/AUC_{nic} .

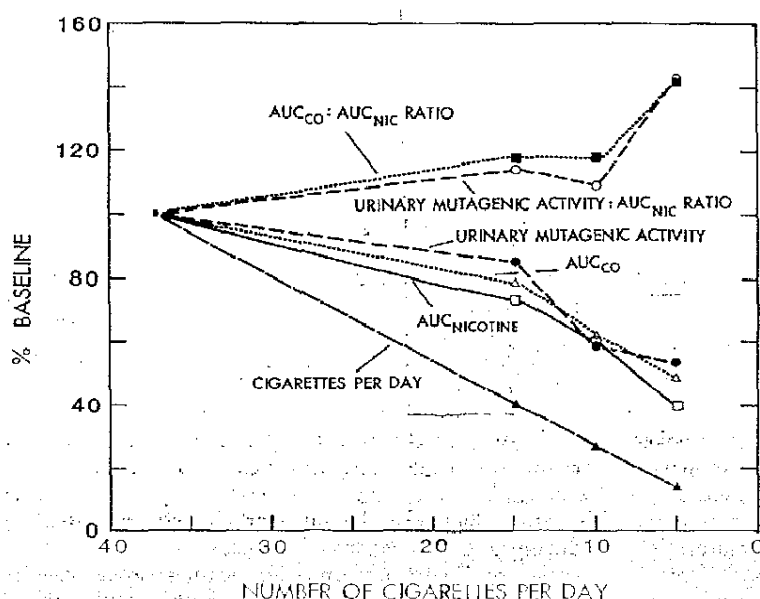


Figure 1. Influence of Reductions in Cigarettes Smoked on Daily Exposure to Tar, Nicotine, and Carbon Monoxide.

Tar was estimated as mutagenic activity of the urine. The data on nicotine and carbon monoxide are mean values for 13 subjects; the data on urinary mutagenicity are mean values for 11 subjects. AUC_{nic} denotes the area under the blood concentration-time curve for nicotine; AUC_{CO} the area under the blood concentration-time curve for carbon monoxide.

the boundary model of nicotine regulation.¹² This model holds that nicotine intake is biologically regulated mainly at the extremes of "too little" or "too much" intake between these boundaries, psychosocial influences (e.g., the cost of cigarettes or requests to reduce consumption), rather than the need for the drug, account for variation in nicotine intake.

Our subjects smoked different numbers of cigarettes for only three or four days. Whether intense oversmoking of cigarettes persists among smokers who restrict their smoking for longer periods is

would have predicted. It was not until the smokers were restricted to smoking five cigarettes per day that the average exposure declined to 50 percent of base line. The finding of increased ratios of urinary mutagenic activity and carbon monoxide to nicotine exposure as fewer cigarettes were smoked is consistent with machine-smoking studies, in which cigarettes are puffed more frequently or more intensely.^{10,11} As cigarettes are smoked to shorter butt lengths, the delivery of tar and carbon monoxide increases logarithmically, whereas the delivery of nicotine increases arithmetically. Thus, each cigarette is smoked in a manner that results in the delivery of tobacco smoke that may have a more toxic composition.

We found significant reductions in exposure to nicotine and carbon monoxide when cigarette intake was reduced by 60 percent (from 37 to 15 cigarettes per day). The number of cigarettes smoked when smoking was unrestricted did not indicate which smokers would benefit the most from reductions in the cigarette ration. The greatest reductions in exposure to toxins were found among smokers with the highest nicotine intake per cigarette when smoking was unrestricted, presumably because they normally smoked cigarettes intensely and had less potential for increasing their intake per cigarette. Our finding that nicotine intake increased per cigarette supports the findings of Ho-Yen et al.,⁶ but our measurements of the area under the blood concentration-time curve show that overall nicotine intake does decline with restrictions on cigarette smoking.

The practical medical benefit of recommending reductions in the number of cigarettes smoked depends on how well smokers comply. The overall pattern of reductions in exposure to nicotine, together with the small number of behavioral problems until severe reductions in nicotine intake were achieved, supports

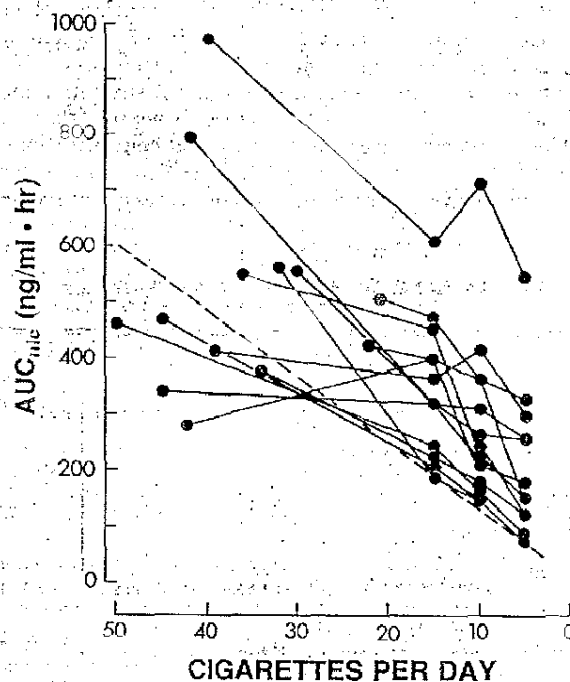


Figure 2. Daily Exposure to Nicotine in 13 Subjects Smoking Different Numbers of Cigarettes.

AUC_{nic} denotes the area under the nicotine blood concentration-time curve. The dashed line indicates the slope of the decline in nicotine exposure that would be expected if nicotine intake were proportional to the number of cigarettes smoked per day.

known. Moreover, our data may not apply to people who themselves choose to smoke fewer cigarettes, on whose smoking patterns the existing data on the dose-disease rate are based. People who choose to smoke fewer cigarettes per day may have a different level of dependence on nicotine.

Our data may not apply to all smokers who are trying to quit. Some smokers may consciously restrain the intensity of their puffing on each cigarette. However, our data are relevant to patients who are asked by their physicians to smoke fewer cigarettes. Such patients could easily cut down from 40 to 15 cigarettes per day while reducing their intake of the toxins in tobacco smoke only slightly, by unknowingly smoking each cigarette more intensely.

Our findings do not contradict the proposition that smoking fewer cigarettes per day poses less risk to health than smoking more cigarettes. However, the magnitude of the benefit from reduced exposure to toxins was much less than expected. Our observations may also explain why some patients in smoking-cessation programs are able to cut down their daily cigarette consumption but are not able to quit smoking successfully. They are presumably able to maintain, to a considerable degree, their level of nicotine dependence even though they are smoking fewer cigarettes.

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